Pharmacoeconomic analysis of voriconazole vs. caspofungin in the empirical antifungal therapy of febrile neutropenia in Australia
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study assessed the cost-benefit of using voriconazole versus caspofungin as first-line antifungal therapy in cancer patients with febrile neutropenia (fever associated with abnormally low numbers of white blood cells). The authors concluded that caspofungin appeared to have a higher probability of being cost-saving than voriconazole. The quality of the study methodology was adequate with appropriate reporting. Given the scope of the analysis, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The study assessed the cost-benefit of using voriconazole versus caspofungin as first-line antifungal therapy in cancer patients with febrile neutropenia (fever above 38°C and neutrophil count below 500 per mm$^3$) who had received parenteral antibacterial therapy for at least 96 hours.

Interventions
First-line antifungal therapy voriconazole was compared with caspofungin. Voriconazole was given as an intravenous loading dose of 6mg/kg twice on day one, followed by twice-daily intravenous doses of 3mg/kg or twice-daily 200mg tablets for a median duration of seven days (range one to 113 days); patients on oral therapy received three days of prior intravenous voriconazole (oral therapy was received by 22% of patients on voriconazole). Caspofungin was given at 70mg on day one, followed by 50mg daily for a median duration of 11 days (range one to 90 days).

Location/setting
Australia/inpatient secondary care.

Methods
Analytical approach:
A decision tree was used to model the costs and outcomes associated with the two interventions. The authors reported that a short-term time horizon was used. The perspective of the study was that of the Australian hospital system.

Effectiveness data:
Clinical and effectiveness data came from previously published studies. An independent expert panel was convened comprising clinicians with experience in fungal therapy to review the evidence considered for the model. The main measure of effectiveness was the treatment success with voriconazole and caspofungin. Antifungal treatment success was defined as a five-point composite endpoint: the absence of breakthrough fungal infection; survival for seven days beyond therapy end; no premature discontinuation of therapy due to side effects or lack of efficacy; resolution of fever; and successful treatment of any baseline fungal infection. These estimates of effectiveness came from two large international multi-centre randomised trials. One trial compared voriconazole with liposomal amphotericin B (Walsh 2002, see Other Publications of Related Interest). A second trial compared caspofungin with liposomal amphotericin B (Walsh 2004, see Other Publications of Related Interest).

Monetary benefit and utility valuations:
Not relevant.
Measure of benefit:
Benefits were measured by treatment success and the probability of survival.

Cost data:
The direct costs included treatment of fungal infections, diagnostic and monitoring tests, medical therapy, concomitant medications, and hospitalisations. Resource use, including hospitalisation, came from the opinion of four clinical experts. Hospitalisation costs were from Australian Refined-Diagnosis Related Groups. Medication costs were based on drug wholesale prices. Other unit costs came from the Australian Medicare Benefits Schedule. Costs were inflated using the Australian consumer price index, when required; they were expressed in 2009/2010 Australian dollars (AUD).

Analysis of uncertainty:
One-way sensitivity analyses were undertaken by varying key model parameters. A probabilistic sensitivity analysis was undertaken using 5,000 Monte Carlo simulations, where each model parameter was fitted with a probability distribution. These results were presented using 95% uncertainty intervals (UI) and a cost-effectiveness acceptability curve.

Results
The average cost per patient was AUD 41,356 (95% UI 37,760 to 45,270) for voriconazole and AUD 40,558 (95% UI 36,870 to 44,290) for caspofungin.

The probability of success was 25.96% (95% UI 24.65 to 27.25) with voriconazole and 34.22% (95% UI 32.50 to 36.00) with caspofungin.

The probability of survival was 92.07% (95% UI 91.53 to 92.58) with voriconazole and 92.63% (95% UI 92.12 to 93.13) with caspofungin.

The authors reported that the results of the probabilistic sensitivity analysis showed that there was a 65.5% probability of caspofungin being cost-saving.

Authors’ conclusions
The authors concluded that caspofungin appeared to have a higher probability of being cost-saving compared with voriconazole.

CRD commentary
Interventions:
The interventions were reported in detail. An expert panel confirmed that the interventions reflected available treatment options in Australia. The feasibility of these options in other settings was unclear.

Effectiveness/benefits:
Clinical and effectiveness data came from published studies, which were reviewed by an expert panel of clinicians. The main measures of effectiveness used came from two randomised controlled trials (RCTs). It was likely that the measures of effectiveness used were internally valid, as well-conducted RCTs that assess the effectiveness of healthcare interventions can be the gold-standard. However, the authors did not report if a systematic review of the literature was undertaken, so all the relevant evidence might not have been considered.

Costs:
The perspective adopted in the economic analysis was explicitly reported to be that of the Australian hospital system. For this perspective, it would appear that all relevant costs were included. The sources from which costs came were adequately reported, as was the price year and currency details. The time horizon, although not explicitly quantified, appeared to be those of the two pivotal RCTs used in the analysis and was short-term (less than a year).

Analysis and results:
A decision tree was used to model cost and outcome information. An incremental approach was appropriately used to synthesise the costs and benefits of the alternative strategies. Adequate details of the model structure were provided, including a diagram. Uncertainty in the results was adequately tested using one-way and probabilistic sensitivity
analyses. The authors reported that the estimation of data based on expert panel opinion was a main limitation of the study.

Concluding remarks:
The quality of the study methodology was adequate with appropriate reporting. Given the scope of the analysis, the authors’ conclusions appear to be valid.

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